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Review article

Intrauterine device use among women with uterine fibroids: a systematic review☆

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Abstract

Background: There are concerns that intrauterine device (IUD) use by women with uterine fibroids might increase their uterine bleeding or risk for device expulsion. The objective of this systematic review was to evaluate evidence concerning the safety and effectiveness of IUD use among women with uterine fibroids. Key questions included whether IUD use is associated with increased risk for uterine bleeding among women with uterine fibroids and whether the presence of uterine fibroids is associated with an increased risk for device expulsion among IUD users.

Study Design: We searched the PubMed database for peer-reviewed articles relevant to IUD (copper or levonorgestrel-releasing) use and uterine fibroids published in any language from database inception through June 2009. We used standard abstract forms and a grading system to summarize and assess the quality of the evidence.

Results: From 202 articles found in the database search, we identified 11 studies that met our inclusion criteria, all of which examined outcomes among users of the levonorgestrel-releasing IUD (LNG-IUD). Evidence from 10 of 11 noncomparative studies (Level II-3, fair) suggests that LNG-IUD use among women with fibroids does not increase menstrual bleeding, and results from all 11 showed that menstrual blood loss decreased among women who continued to use the LNG-IUD through the end of the study period. Overall, serum levels of hemoglobin, hematocrit and ferritin increased among LNG-IUD users in studies that assessed these outcomes. Several studies reported some occurrences of irregular bleeding. Findings from two cohort studies (Level II-2, fair to poor) showed rates of LNG-IUD expulsion to be higher among women with uterine fibroids (11% in each) than among women without uterine fibroids (0% and 3%); however, in one study the difference was not statistically significant, and in the other significance testing was not conducted. Six prospective noncomparative studies reported expulsion rates of 0–20% among women with uterine fibroids.

Conclusions: Most women with uterine fibroids are likely to have less menstrual blood loss and higher serum levels of hemoglobin, hematocrit and ferritin after insertion of an LNG-IUD, despite some occurrences of irregular bleeding. LNG-IUD users with uterine fibroids may have higher rates of expulsion than those without fibroids.

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Keywords: Intrauterine device; Uterine fibroid; Leiomyoma; Uterine bleeding; Expulsion

1. Introduction

Uterine fibroids, or leiomyomata, are benign tumors of smooth muscle origin that may produce symptoms including menorrhagia, dysmenorrhea, pelvic pressure, and pain and reproductive dysfunction, although most women with uterine fibroids have no symptoms [1–3]. The pathogenesis of fibroids remains unclear, although fibroid growth is thought to be related to genetics, steroid hormones and growth factors important in fibrotic processes and angiogenesis [4]. In the United States, uterine fibroids have been estimated to be clinically evident in 20–50% of reproductive-age women [5,6], although results from a population-based study in which fibroid screening was conducted via transvaginal ultrasound showed that the cumulative incidence of uterine fibroids by age 50 was nearly 70% among

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white women and >80% among black women [7]. Black women are nearly three times as likely to develop uterine fibroids as white women and to develop their fibroids at an earlier age [7].

Changes in uterine bleeding are a common occurrence with intrauterine device (IUD) use. Given that uterine fibroids are commonly associated with heavy menstrual bleeding, there is concern that IUD use may worsen uterine bleeding patterns experienced by women with fibroids and that fibroids may increase IUD users' risk for IUD expulsion. In this systematic review, we evaluate evidence concerning the safety and effectiveness of IUD use by women with uterine fibroids; specifically, whether IUD use is associated with an increased risk for uterine bleeding among women with uterine fibroids and whether the presence of uterine fibroids is associated with an increased risk for IUD expulsion among IUD users.

2. Materials and methods

We searched the PubMed database for peer-reviewed articles concerning the safety or effectiveness of IUD use among women with uterine fibroids published in any language from database inception through June 2009. We also searched the Cochrane Library for relevant systematic reviews and searched reference lists from articles identified in the search. We did not consider abstracts of conference presentations. Our search strategy is described more fully in Appendix A.

2.1. Study selection

We reviewed titles as well as abstracts to identify studies investigating the safety or effectiveness of IUD use by women with uterine fibroids. We included studies that examined uterine bleeding outcomes and device expulsion among IUD users with uterine fibroids but excluded studies that evaluated the risk of developing uterine fibroids among IUD users [8] and those that solely examined the relationship between IUD use among women with uterine fibroids and outcomes supplementary to the objectives of our review (e.g., fibroid size) [9]. We excluded case reports but included all other study designs. We also excluded four prospective noncomparative studies with overlapping samples of women, some of whom had uterine fibroids, which examined menstrual blood loss and IUD expulsion among women using the frameless FibroPlant-levonorgestrel intrauterine device [10–13], given that the device is not approved for use in the United States.

2.2. Study quality assessment

We summarized and systematically assessed the evidence using standard abstract forms [14] and assessed the quality of each piece of evidence using the United States Preventive Services Task Force grading system [15]. Our primary safety outcome was uterine bleeding, and our primary effectiveness outcome was IUD expulsion. In studies of IUD-associated risk for uterine bleeding, we considered women with uterine fibroids not using an IUD to be the appropriate comparison group, and in studies of fibroid-associated risk for IUD expulsion, we considered IUD users without uterine fibroids to be the appropriate comparison group. Thus, a study that examined both uterine bleeding outcomes and expulsion rates may have received different quality ratings based on the appropriateness of the comparison group for each research question.

2.3. Data synthesis

We did not compute summary measures of association for the 11 studies we reviewed because of differences in how they reported outcomes, in the populations they studied, and in the length of their follow-up.

3. Results

The search strategy identified 202 possibly relevant articles. After reviewing the titles and abstracts of these articles, as well as the full articles when necessary, we determined that eight articles met our criteria for inclusion in this review [16–23]. We also found three additional articles that met our inclusion criteria by hand-searching references [24–26]. We found no relevant systematic reviews in our search of the Cochrane database.

Each of the 11 studies included examined outcomes associated with use of the LNG-IUD (20 mcg/day). We did not identify any studies on the safety or effectiveness of the copper-bearing IUD in women with uterine fibroids. One study examining uterine bleeding outcomes among LNG-IUD users with uterine fibroids used women with uterine fibroids treated with thermal balloon ablation as a comparison group [21]; however, because we were primarily interested in the safety of LNG-IUD use among women with uterine fibroids and not in comparative treatment effects of the LNG-IUD versus other treatments, we did not consider this group as a comparison group for our purposes.

All 11 studies examined uterine bleeding outcomes among LNG-IUD users and were noncomparative, meaning that they did not include a comparison group of women with uterine fibroids not using an IUD. We classified 10 of the 11 as prospective noncomparative studies [16–23,25,26] and one as a retrospective noncomparative study [24]. Eight of these studies were exclusively among women with uterine fibroids [16,17,19–22,25,26], and three were among women with menorrhagia, some of whom also had uterine fibroids [18,23,24]. Our main safety indicators were changes in menstrual blood loss and in serum levels of hemoglobin, hematocrit, and ferritin; however, we also note occurrences of irregular bleeding when discussed in the studies.

Eight of the 11 studies also reported expulsion rates [16,17,19–21,24–26]. Two of these were cohort studies, one